```
=> d his

     (FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
     AT 15:05:37 ON 25 JUL 2003)
               DEL HIS
L1        602904 S EPITHELI?
L2        224048 S RETINA?
L3         23372 S L1 (L) L2
L4           125 S L3 AND IMMORTAL?
L5            66 S L4 AND NON?
L6            33 DUP REM L5 (33 DUPLICATES REMOVED)
L7            33 SORT L6 PY
L8             0 S L7 AND MICRON
L9             0 S L7 AND MICRON?
L10            0 S L7 AND SIZE
L11          158 S L3 AND MICRON?
L12          145 DUP REM L11 (13 DUPLICATES REMOVED)
L13          145 FOCUS L12 1-
L14         3893 S L1 AND MICRON?
L15           49 S L14 AND (CELL SIZE)
L16           41 DUP REM L15 (8 DUPLICATES REMOVED)
L17           35 S L16 AND PY<=1998
L18            1 S L17 AND RETINA?
                 E QUINONERO JEROME?/AU
L19           30 S E1
                 E GREEWOOD JOHN?/AU
                 E GREENWOOD JOHN?/AU
```

L17 ANSWER 5 OF 35 MEDLINE on STN
AN 97362822 MEDLINE
TI Size of cells collected from normal human subjects using contact lens cytology.
SO OPTOMETRY AND VISION SCIENCE, **(1997 May)** 74 (5) 280-7.
Journal code: 8904931. ISSN: 1040-5488.
AU Laurent J; Wilson G
AB This paper describes how a soft contact lens can be used to harvest cells from the surface of the corneal **epithelium**. The procedure is called contact lens cytology (CLC). Cells were removed from a soft contact lens by irrigation and stained with acridine orange. Two methods for the measurement of **cell size** are described. First, **cell size** was measured using a computer-assisted technique, which calculated the area of the cell from its outline. The second method was simpler in that it required only a single measurement of the longest dimension of the cell (the cell length). To test the validity of this simpler method, cell area was compared with cell length in 185 cells. The resulting correlation (r = 0.92) suggests that the size of shed cells can be described adequately using cell length in place of the more time-consuming measurement of cell area. A mathematical relation can be used to convert cell length to cell area so that results from experimenters using different measures of size can be compared. When a large pool of cells collected by CLC was divided into four aliquots and cell length measured by two observers on two different days, there were no significant differences between observers or days. Thus, the technique does not depend on one observer, and it is unaffected by a 24-h delay in measurement. Cells were harvested from the corneal **epithelium** of normal human subjects. The number of cells collected from any single removal of the contact lens had a range of 10 to 175 cells, and a mean of 66.8 +/- 40.4 (N = 46). Cell length was measured and plotted as frequency histograms for both eyes of each subject. The range in cell length was from 10 to 80 **microns**. The mean cell length for individual subjects had a low of 26.5 +/- 9.0 **microns** and a high of 44.2 +/- 10.2 **microns**, with a grand mean for all right eyes of 36.0 +/- 5.1 **microns**, and a grand mean for all left eyes of 34.6 +/- 5.2 **microns**. The mean for all eyes was 35.3 +/- 5.1 **microns**. Composite histograms were created with the combined data from the 23 right eyes (N = 1310 cells), and the 23 left eyes (N = 1765 cells). Individual histograms and the composite histograms were not normally distributed. Peaks in the distributions suggest the presence of different subpopulations of cells, lending support to the hypothesis that there is more than one mechanism for cell shedding.

ANSWER 2 OF 33 MEDLINE on STN
AN 93194973 MEDLINE
TI **Immortalization** of polarized rat **retinal** pigment **epithelium**.
SO JOURNAL OF CELL SCIENCE, (1993 Jan) 104 (Pt 1) 37-49.
Journal code: 0052457. ISSN: 0021-9533.
AU Nabi I R; Mathews A P; Cohen-Gould L; Gundersen D; Rodriguez-Boulan E
AB Rat **retinal** pigment **epithelial** (RPE) cells were **immortalized** by infection with a temperature-sensitive tsA SV40 virus and following cloning and selection for **epithelial** properties the polarized RPE-J cell line was obtained. At the permissive temperature of 33 degrees C, RPE-J cells behave as an **immortalized** cell line. When RPE-J cells are grown on nitrocellulose filters coated with a thin layer of Matrigel in the presence of 10(-8) M retinoic acid for 6 days at 33 degrees C and then switched for 33-36 hours to the **non**-permissive temperature of 40 degrees C, they acquire a differentiated polarized RPE phenotype. Under these growth conditions, RPE-J cells exhibit circumferential staining for the tight-junction protein ZO-1 and acquire a transepithelial resistance of 350 ohms cm2. Morphologically, RPE-J cells exhibit a characteristic RPE morphology with extensive apical microvilli as well as numerous dense bodies including premelanosomes and varied multilamellar structures. Ruthenium red labeling revealed the frequent basal localization of the tight junction. The cells were identified to be of rat RPE origin by their expression of the rat RPE marker RET-PE2 and their ability to phagocytose latex beads. While RPE-J cells are capable of sorting influenza and vesicular stomatitis virus to the apical and basal surfaces, respectively, the Na,K-ATPase is not polarized and the neural cell adhesion molecule, N-CAM, is localized exclusively to the lateral surface. In vivo the apical surface of RPE interacts with the adjacent neural **retina** and the Na,K-ATPase and N-CAM are both apical; the altered polarity of these two proteins in RPE-J cells may be a consequence of the absence of apical interaction with the neural **retina** in culture. Previous studies of RPE have been restricted to the use of primary cultures and the RPE-J cell line should prove an excellent model system for the study of the mechanisms determining the characteristic polarity and functions of the **retinal** pigment **epithelium**.

L7 ANSWER 3 OF 33 MEDLINE on STN
AN 93178557 MEDLINE
TI Spontaneously arising **immortal** cell line of rat **retinal** pigmented **epithelial** cells.
SO EXPERIMENTAL CELL RESEARCH, (1993 Feb) 204 (2) 311-20.
Journal code: 0373226. ISSN: 0014-4827.
AU McLaren M J; Sasabe T; Li C Y; Brown M E; Inana G
AB A continuous cell line of rat **retinal** pigment **epithelium** (RPE), named BPEI-1, has been established and characterized. Sheets of pure RPE cells, uncontaminated by choroidal or neural **retinal** cell types, were isolated from eyes of 7-day-old Long Evans rats and established in primary culture. The primary RPE cells became extensively spread and grew slowly for approximately 1 month, at which time a colony of small rapidly dividing cells spontaneously appeared. Following trypsinization, most of the typical primary RPE cells did not survive and were quickly outnumbered by the smaller cells, which gave rise to a cell line that was grown continuously for several hundred generations. When growing at the maximal rate in media containing 20% FBS (doubling time 18 h), the cells were fibroblastic and nearly devoid of pigment, but were capable of morphologic transition back to a pigmented, **epithelioid** form when cultured under low serum conditions. Evidence that these cells originated from RPE included specific immunolabeling with antibodies to cellular **retinaldehyde** binding protein and cytokeratin, negative GFAP immunoreactivity, and demonstration of avid phagocytosis of isolated rod outer segments by these cells. Partial characterization of choroidal cells eliminated the latter cells as possible contaminants which could have given rise to the cell line. The BPEI-1 cell line, and other rat RPE cell lines currently being developed from pigmented normal (LE, RCS rdy+p+) and **retinal** dystrophic (RCS p+) rats should facilitate biochemical and molecular biological approaches to study of RPE cell function in health and disease.

L4 ANSWER 2 OF 2 MEDLINE on STN
AN 83278727 MEDLINE
TI Retinal photoreceptor fine structure in the domestic sheep.
SO ACTA ANATOMICA, (1983) 116 (3) 265-75.
Journal code: 0370272. ISSN: 0001-5180.
AU Braekevelt C R
AB The structure of the photoreceptors of the domestic sheep has been investigated by light and electron microscopy. In the sheep retina the photoreceptors are readily differentiated and adequately described by the classical terminology of rods and cones. Rods are more numerous then cones. They appear as tall slender cells measuring 45-50 **microns** in length and 2-3 **microns** in diameter with inner and outer segments of the same diameter. Rod nuclei are located at all levels of the outer nuclear layer. The rod synaptic ending is small and rounded with two to three invaginated (ribbon) synaptic sites. Cone cells are shorter than rods, measuring only 30-35 **micron** in total length. The cone inner segment is wider than the outer segment which tapers distally. Cone nuclei are located adjacent to the external limiting membrane and are more vesicular than rod nuclei. Cone synaptic endings are larger spherules with ten to twelve (ribbon) synaptic sites. Both rods and cones also display superficial synaptic regions. An unusual form of apparent degeneration is noted in cone photoreceptors. This involves a disorganization and loss of the outer segment and a progressive distal movement of the nucleus through the inner segment towards the **retinal epithelial** layer. The structure and ratio of rods and cones remains similar in both the tapetal and nontapetal regions of the fundus.

L15 ANSWER 9 OF 35 MEDLINE on STN
AN 81222106 MEDLINE
TI **Retinal pigment epithelial** abnormalities in fundus flavimaculatus: a light and electron microscopic study.
SO OPHTHALMOLOGY, (1980 Dec) 87 (12) 1189-200.
Journal code: 7802443. ISSN: 0161-6420.
AU Eagle R C Jr; Lucier A C; Bernardino V B Jr; Yanoff M
AB Light, fluorescent, and scanning and transmission electron microscopic examinations of two postmortem eyes from a 24-year-old man with well-documented fundus flavimaculatus with atrophic macular degeneration revealed striking abnormalities in the retinal pigment epithelium (RPE). Beginning near the equator, scanning electron microscopy demonstrated a progressively marked heterogeneity in the size of the RPE cells. Surrounded by a fairly regular mosaic of relatively normal appearing cells, enormously enlarged hypomelanotic cells measuring up to 80 **microns** in diameter occurred in irregular aggregates that became more prevalent posteriorly. Diffusely and intensely PAS-positive, the RPE was packed with a granular substance with ultrastructural, autofluorescent, and histochemical properties consistent with an abnormal form of lipofuscin. The greatest concentration of lipopigment was noted posteriorly. Stains for acid mucopolysaccharide were only mildly positive. The clinical and fluorescein angiographic manifestations of fundus flavimaculatus are consistent with accumulation of a lipofuscin-like substance in the RPE. The massive amounts of lipopigment encountered in this young individual suggest that disordered lipopigment metabolism may play a major role in the pathogenesis of this **retinal pigment epithelial** disorder.

ANSWER 7 OF 7 SCISEARCH COPYRIGHT 2003 THOMSON ISI

AN 2002:408487 SCISEARCH

TI Vascular morphogenesis and differentiation after adoptive transfer of human endothelial cells to immunodeficient mice

SO AMERICAN JOURNAL OF PATHOLOGY, (MAY 2002) Vol. 160, No. 5, pp. 1629-1637.
Publisher: AMER SOC INVESTIGATIVE PATHOLOGY, INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3993 USA.
ISSN: 0002-9440.

AU Skovseth D K (Reprint); Yamanaka T; Brandtzaeg P; Butcher E C; Haraldsen G

AB To establish a model for adoptive transfer of **endothelial** cells, we transferred human umbilical vein **endothelial** cells (HUVECs) to immunodeficient mice (Rag 2(-/-)). HUVECs were **suspended** as **single cells** in Matrigel and injected subcutaneously in the abdominal midline. Within 10 days after injection, HUVECs expressed pseudopod-like extensions and began to accumulate in arrays. By day 20, we observed human vessels that contained erythrocytes, and on day 30 we observed perivascular cells that expressed smooth muscle actin, thus resembling mature vessels. Throughout the experimental period, HUVECs bound Ulex europaeus lectin and expressed CD31, VE-cadherin, von Willebrand factor, as well as ICAM-2. A fraction of the cells also expressed the proliferation marker Ki67. Moreover, the sialomucin CD34, which is rapidly down-regulated in cultured HUVECs, was reinduced in vivo. However, we found no reinduction of CD34 in cells cultured inside or on top of Matrigel in vitro. We also injected cells **suspended** in Matrigel around the catheter tip of implanted osmotic pumps. Delivery of recombinant human interferon-gamma by this route led to strong induction of MHC class II and ICAM-1 on the human vessels. In conclusion, isolated human **endothelial** cells can integrate with the murine vascular system to form functional capillaries and regain in vivo properties.

ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1999:708494 CAPLUS
DN 131:308610
TI Cell culturing method and medium for producing proliferated, normal, differentiated human liver cells
SO Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
IN Curcio, Francesco; Coon, Hayden G.; Ambesi-Impiombato, Francesco Saverio
AB The present invention provides improvements in a method for producing an expanded non-transformed cell culture of human liver cells comprising the steps of: (1) prepg. partially purified, minced human liver tissue, (2) concg. the resulting cells and tissue pieces, (3) resuspending the concd. tissue cells and pieces in a growth medium, (4) culturing the resuspended cells in the growth medium for a time and under conditions to effect sustained cell division, and (5) passaging the cultured human liver cells periodically to expand the culture. The growth medium comprises a combination of a basal medium and ingredients to provide a medium in which the cultured human liver cells are selectively proliferated without being transformed, providing an expanded culture of proliferated, functionally differentiated human liver cells that is substantially free of fibroblast, macrophage and capillary **endothelial** cells, the improvement comprising the steps of harvesting cells of the expanded culture at a selected population doubling level (PDL) preferably >5, providing a high d. cell **suspension** of such proliferated human liver cells, and incubating such high d. cell **suspension** in a calm-down medium to induce a mitotically quiescent state and, using a culture procedure which encourages aggregation, making the cells adhere tightly to form a three-dimensional cell organization typical of the organ of origin, thereby forming organoids. Methods of gel-embedding the **single cells**, aggregates and organoids produced by the method; the growth medium and calm-down medium; various different methods for use of the normal, proliferated human liver cells produced by the method, are also provided.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 953633	A1	19991103	EP 1999-303337	19990428
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	WO 9423572	A1	19941027	WO 1994-US3101	19940321
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2159804	AA	19941027	CA 1994-2159804	19940321
	AU 9464139	A1	19941108	AU 1994-64139	19940321
	AU 687386	B2	19980226		
	JP 08506735	T2	19960723	JP 1994-523199	19940321
	US 5646035	A	19970708	US 1995-480149	19950607
	US 5780299	A	19980714	US 1995-480027	19950607
	US 5849584	A	19981215	US 1995-485650	19950607
	US 5888816	A	19990330	US 1995-480022	19950607
	US 6008047	A	19991228	US 1998-66897	19980428

L6 ANSWER 3 OF 7 MEDLINE
AN 91125862 MEDLINE
TI Cell type-specific tumor induction in neural transplants by retrovirus-mediated oncogene transfer.
SO ONCOGENE, (1991 Jan) 6 (1) 113-8.
Journal code: 8711562. ISSN: 0950-9232.
AU Aguzzi A; Kleihues P; Heckl K; Wiestler O D
AB Using a neural transplantation model which mimics structural and functional properties of the normal rat **brain** to a high extent, we have taken a novel approach to study the transforming potential of activated oncogenes in the developing **brain**. **Single cell suspensions** prepared from fetal rat **brains** were infected with replication-defective retroviral vectors encoding oncogenes and stereotaxically injected into the caudoputamen of adult F344 rats. Rats carrying transplants expressing the polyoma middle T antigen developed **endothelial** hemangiomas in the graft which in 70% of the recipient animals led to fatal **cerebral** hemorrhage within 13-50 days after transplantation. Expression of the v-src gene caused astrocytic and mesenchymal tumors with a 70% incidence after latency periods of 2-6 months, but no **endothelial** lesions. It was found by in situ hybridization that these oncogenes are expressed in all cell types present in the graft. This indicates that cell-type specific transformation is due to differential susceptibility of the respective target cell to the oncogenes, rather than selective integration or expression of the retroviral construct. The highly efficient gene transfer by retroviral vectors into fetal **brain** transplants provides a challenging experimental strategy to study differentiation and oncogenesis in the CNS.

ANSWER 2 OF 7 MEDLINE

AN 90035244 MEDLINE

TI Tumour induction in fetal **brain** transplants exposed to the viral oncogenes polyoma middle T and v-src.

SO IARC SCIENTIFIC PUBLICATIONS, (1989) (96) 267-74.
Journal code: 8009542. ISSN: 0300-5038.

AU Wiestler O D; Aguzzi A; Williams R L; Wagner E F; Boulter C A; Kleihues P

AB Using a neural transplantation model, we have studied the effect of polyoma virus middle T antigen and of the viral src oncogene on the developing rat **brain**. For this purpose, **single-cell suspensions** of fetal rat **brain** were prepared on day 14 of gestation (E14), infected with a replication-defective retroviral vector which carries the middle T oncogene driven by an internal thymidine kinase promoter, and stereotaxically injected into the caudoputamen of adult host rats. With mock-infected donor cells, the transplants developed into an organotypically differentiated population of neurons, astrocytes, oligodendrocytes and other central nervous system cell types and expressed marker proteins of mature neuroectodermal cells, including neuron-specific enolase, synaptophysin, neurofilament protein, glial fibrillary acidic protein and S-100 protein. A high percentage of rats carrying transplants infected with the middle T-encoding vector died within two to six weeks from massive haemorrhage into the transplant. Upon microscopic examination, gross abnormalities of the microvasculature were seen, with formation of large blood-filled spaces lined by a thin layer of proliferating **endothelial** cells. This effect of middle T was apparently cell type-specific, since the differentiation of neuroectodermal cells within the graft proceeded in a regular fashion. In order to assess further the cell-specificity of the oncogene, analogous experiments were carried out with a retroviral construct in which the middle T cDNA had been replaced by the viral src gene (v-src). Transplants infected with the v-src vector developed astrocytomas, but no vascular abnormalities. (ABSTRACT TRUNCATED AT 250 WORDS)

L13 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2003 ACS
AN 2001:816875 CAPLUS
DN 135:341193
TI Immortalized lines of endothelial brain cells and therapeutic application thereof
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
IN Chaverot, Nathalie; Couraud, Pierre-Oliver; Laterra, John; **Quinonero, Jerome**; Roux, Francoise; Strosberg, Arthur Donny
AB The invention relates to optionally modified immortalized lines of endothelial brain cells of mammalians, as well as applications as preventive or curative drug, and particularly for the treatment of primary and secondary, neurol. or psychiatric diseases, including Alzheimer's disease, Huntington's disease, Amyotrophic Lateral Sclerosis (Lou Gehrig's disease), Parkinson's disease, glioblastoma and other brain tumors, and stroke. The invention also relates to the method for prepg. the cell lines. The endothelial cell lines of mammalians disclosed are comprised of immortalized endothelial brain cells presenting characteristics of differentiated endothelial brain cells, in a stable way. The cell lines comprise a nucleic acid having at least one immortalizing viral or cellular oncogene, optionally assocd. with at least one selection gene, and an expression vector comprising a sequence coding for polypeptide, a protein, or a viral vector, optionally assocd. with at least one selection gene and optionally at least one marker gene, and they are capable in vivo to integrate brain vessels of a host mammalian and produce said polypeptide, the protein or the viral vector.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001083716	A2	20011108	WO 2001-US14286	20010503
WO 2001083716	A3	20020606		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

L13 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2003 ACS
AN 2000:441659 CAPLUS
DN 133:63922
TI Single cell-suspensions of transgenic animal cells for use in gene therapy without a risk of blocking minor vessels
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
IN Timsit, Serge; **Quinonero, Jerome**
AB Suspensions of mammalian cells transformed with a therapeutic gene with the cells forming very few or no aggregates are described for use in gene therapy by systemic administration. The invention is characterized in that it does not comprise aggregate of said cells having a size likely to cause temporary or permanent dysfunction in the subject. The invention also concerns pharmaceutical compns. comprising said prepn. and an acceptable carrier. Cultured transgenic cells were suspended by trypsinization and mixed by vigorous pipeting with a diluent before filtration through a 30 .mu. pore size filter. The final suspension had a cell d. of 1,000-300,000 per .mu.L. Rats infused with such cells were studied for the effects of the infusion. Of 48 rats, 4 died of respiratory or neurol. complications and one died of unknown causes. The remaining animals showed no ill effects and the infused cells became rapidly distributed throughout the brain.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000037111	A1	20000629	WO 1999-FR2964	19991130
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2787463	A1	20000623	FR 1998-16144	19981221
FR 2787463	B1	20010330		
CA 2355882	AA	20000629	CA 1999-2355882	19991130
EP 1140207	A1	20011010	EP 1999-973473	19991130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532117	T2	20021002	JP 2000-589221	19991130

L13 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2003 ACS
AN 2000:441660 CAPLUS
DN 133:53709
TI Pharmaceutical compositions comprising immortalized endothelial cells for use in the diagnosis and treatment of sources of angiogenesis
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
IN Timsit, Serge; **Quinonero, Jerome**
AB The invention discloses a pharmaceutical compn. to be used for diagnosing and/or treating angiogenic sources by being administered to a subject by systemic administration, the compn. contg.immortalized mammalian endothelial cells, optionally having an active substance for diagnosing and/or treating angiogenic sources.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000037112	A1	20000629	WO 1999-FR2965	19991130
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2787464	A1	20000623	FR 1998-16145	19981221
FR 2787464	B1	20030110		
CA 2355879	AA	20000629	CA 1999-2355879	19991130
EP 1140208	A1	20011010	EP 1999-973474	19991130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532567	T2	20021002	JP 2000-589222	19991130

L13 ANSWER 18 OF 22 MEDLINE
AN 97226860 MEDLINE
TI Gene transfer to the central nervous system by transplantation of cerebral endothelial cells.
SO GENE THERAPY, (1997 Feb) 4 (2) 111-9.
Journal code: 9421525. ISSN: 0969-7128.
AU **Quinonero J**; Tchelingerian J L; Vignais L; Foignant-Chaverot N; Colin C; Horellou P; Liblau R; Barbin G; Strosberg A D; Jacque C; Couraud P O
AB A cerebral endothelial immortalized cell line was used in transplantation experiments to deliver gene products to the adult rat brain. Survival of grafted cells was observed for at least 1 year, without any sign of tumor formation. When genetically modified to express bacterial beta-galactosidase and transplanted into the striatum, these cells were shown, by light and electron microscope analysis, to integrate into the host brain parenchyma and microvasculature. Following implantation into the striatum and nucleus basalis of adult rats, endothelial cells engineered to secrete mouse beta-nerve growth factor (NGF) induced the formation of a dense network of low-affinity NGF receptor-expressing fibers near the implantation sites. This biological response was observed from 3 to 8 weeks after engraftment. The present study establishes the cerebral endothelial cell as an efficient vector for gene transfer to the central nervous system.

19
16
18
20
21
22

L13 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2003 ACS
AN 1996:382921 CAPLUS
DN 125:50738
TI Immortalized lines of brain endothelial cells and therapeutic applications thereof
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
IN Chaverot, Nathalie; Couraud, Pierre-Olivier; Laterra, John; **Quinonero, Jerome**; Roux, Francoise; Strosberg, Arthur Donny; Tchelingerian, Jean-Leon; Vignais, Lionel
AB The invention relates to optionally modified immortalized lines of brain endothelial cells of mammals, as well as applications as preventive or curative drugs and particularly for the treatment of primary and secondary neurol. or psychiatric diseases, including brain tumors, and for stimulating the growth and reprodn. of breeding animals. The invention also relates to the method for prepg. said cell lines. The endothelial cell lines of mammalians disclosed are comprised of immortalized brain endothelial cells presenting at least one of the following characteristics of differentiated endothelial brain cells, in a stable way: the expression of endothelial markers, the secretion of vasoactive substances, the expression of mols. of the major histocompatibility complex (MHC), the expression of hormonal receptors, and the existence of tight junctions. Said cell lines comprise a nucleic acid fragment having at least one immortalizing fragment of a viral or cellular oncogene, optionally assocd. with at least one selection gene, and an expression vector comprising a sequence coding for a polypeptide, a protein or a viral vector, optionally assocd. with at least one selection gene and optionally at least one marker gene. The cell lines are capable of integrating into brain vessels of a host mammal and producing said polypeptide, protein or viral vector. Rat bran endothelial cells were immortalized by transfection with plasmid pE1A-neo, encoding the adenovirus E1A gene. Cell line RBE/NGF, expressing mouse .beta.-nerve growth factor (.beta.-NGF), was prepd. using retroviral vector pMoMuLVisisNGF. These cells were implanted into rat brains. The grafts were not rejected, produced .beta.-NGF, and induced a biol. effect.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9611278	A1	19960418	WO 1995-FR1313	19951009
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2726005	A1	19960426	FR 1994-12078	19941010
FR 2726005	B1	19970103		
CA 2202066	AA	19960418	CA 1995-2202066	19951009
AU 9536575	A1	19960502	AU 1995-36575	19951009
AU 715289	B2	20000120		
EP 787197	A1	19970806	EP 1995-934188	19951009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10507074	T2	19980714	JP 1996-512390	19951009

L13 ANSWER 14 OF 22 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 95:652122 SCISEARCH
TI AN IMMORTALIZED BRAIN ENDOTHELIAL-CELL LINE AS A VECTOR FOR GENE-THERAPY OF NEUROLOGICAL DISORDERS
SO JOURNAL OF CELLULAR BIOCHEMISTRY, (10 MAR 1995) Supp. 21A, pp. 390. ISSN: 0730-2312.
AU COURAUD P O (Reprint); **QUINONERO J**; TCHELINGERIAN J L; VIGNAIS L; JACQUE C; STROSBERG A D